Active mechanism locks in the size of a cell's nucleus

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Cells know that size matters, especially when it comes to the nucleus. In the early 1900s, German scientists first proposed that the size of a nucleus is always proportional to the size of its cell. Now, more than a century later, researchers at Rockefeller University show that an active mechanism controls this process. This mechanism, however, doesn’t reside within the nucleus as many once thought, but instead comes from the cell’s cytoplasm.

In a series of experiments, coauthor Frank Neumann, together with Paul Nurse, head of the Laboratory of Yeast Genetics and Cell Biology, found that regardless of the size or shape of fission yeast, the volume of its nucleus hovers around eight percent — a volume that not only remains constant throughout development, but also resists change, in a wide range of experimental and natural conditions. These findings, which appear in the November 19 issue of the Journal of Cell Biology, raise the question of why cells keep such close tabs on the size and shape of their nuclei.

To test whether the amount of DNA influences the nucleus’s size, Neumann and Nurse genetically manipulated the fission yeast so that the amount of DNA within the nucleus doubled with each cell cycle without the nucleus ever dividing. Nuclei with as much as 32 times more DNA than other nuclei maintained the same nucleus-to-cell ratio, a finding that dispelled the theory that it is the amount of DNA and how tightly it is packed that determines the nucleus’s size. “This was perhaps our most surprising finding,” says Neumann, “that DNA is not what is measured to determine nuclear size." The researchers also found that fission yeast do not measure cell length to lock in this nucleus-to-cell ratio.

Rather, Neumann and Nurse show that it's what's outside the nucleus — not inside it — that determines the size of the nucleus. This time, they confirmed this finding not by doubling the amount of DNA within the nucleus, but the number of nuclei within the fission yeast — single-cell organisms that look like long, straight rods. In this experiment, each cell had four unevenly distributed nuclei.

During cell growth, the volume of each nucleus became directly proportional to the amount of "surrounding" cytoplasm. Particularly, the two nuclei at the ends of the rods, which were surrounded by relatively more cytoplasm, grew faster than the two nuclei between them. When Neumann and Nurse repositioned nuclei to areas with relatively more cytoplasm, the previously small nuclei grew faster than the others until the proper ratio was achieved.

The researchers saw the same results when they genetically modified the multi-nucleated cells to sprout an arm. The nuclei that were close to this junction increased in size since the relative amount of cytoplasm had now increased. Taken together, these experiments suggest that components within the cytoplasm, not DNA content of the nucleus, play an important role in nuclear size control.

When Neumann and Nurse modified the fission yeast cells such that nuclei occupied two times more of the cell volume, the nuclei didn't shrink but "waited" until the cell became sufficiently large before they started to grow.

Likewise, a nucleus that occupied less than eight percent of the cell's volume grew faster than it would have had its nucleus-to-cell ratio not been modified, suggesting that nuclear growth is not directly coupled to cell growth; rather, the nucleus can sense changes to the ratio and adjust its growth accordingly. “These findings provide the first hint of a mechanism and are the basis of uncovering the molecular mechanism of how a cell senses its nucleus’s size,” says Neumann.

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